

### **REMARKS**

The Examiner provides a number of objections and rejections. We list them here in the order in which they are addressed.

I. Claims 1, 9 and 11-12 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Little *et al.* (U.S. Patent No. 6,207,370) in view of Garvin *et al.* (U.S. Patent No. 6,329,180) and further in view of Knop *et al.*

II. Claims 1, 9 and 11-13 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Little *et al.* (U.S. Patent No. 6,207,370) in view of Garvin *et al.* (U.S. Patent No. 6,329,180) further in view of Knop *et al.* and Elion *et al.*

Applicants respond as follows:

**I. Claims 1, 9 and 11-12 are not unpatentable under 35 U.S.C. §103(a).**

The Claims are rejected as obvious on the basis of a combination of Little and Garvin, taken with Knop *et al.* The Examiner admitted (in the prior final office action) that neither Little nor Garvin teach a primer with two epitope markers. The Examiner attempts to remedy this deficiency with Knop *et al.*

The Applicants cannot agree that Knop remedies this deficiency even if this combination of references is made. Specifically, the Applicants contend that the Examiner has misinterpreted the teaching of Knop *et al.* As an introductory point, the 3HA and 6HA tags never appear in the same molecule. This is clearly indicated in Table 1 (page 965) of Knop *et al.*, where the column labeled “tag” lists either 3HA or 6HA – not both. Indeed, as indicated above, since they serve identical purposes there would be no point in including both in the same molecule. Second, these tags NEVER appear in a PCR primer (individually, let alone together). This confusion seems to stem from the column labeled “PCR-primer,” which indicates that 3HA-1 and 3HA-2 primers were used to generate the two products comprising 3HA tags, while T1-TRP1 and T2-TRP1 primers were used to generate the product that comprises the 6HA tag. As indicated in Table 2 (page 966), none of these primers include (any) repetitive histidine codons (i.e. CAC or CAT). These primers merely amplify DNA sequences that contain either 3HA or 6HA tags.

Regardless, in the interest of furthering prosecution and underscoring one embodiment, and without waiving the above arguments, the Applicants have amended Claims 1 and 9 such that they further distinguish over the presently cited references (while preserving the right to prosecute the unamended, or similar, claims in the future). Specifically, Claims 1 and 9 now recite all 3 epitopes as encoding distinct epitopes from one another. Furthermore, dependent claims 38 and 41 further distinguish the location of the first and second epitopes relative to the start codon – an element that is not mentioned by the genomic insertion primers of Knop *et al.* Similarly, Claim 40 indicates the location of the third epitope relative to the stop codon.

Support for the location of the first, second and third epitope markers relative to the start and stop codons, respectively, may be found throughout the specification. For example, page 46, lines 23-30 states that the N-terminal marker, affinity marker and C-terminal marker epitopes are incorporated into the nascent protein. Similarly, page 47, lines 22-30 indicate that the location of each epitope marker permits its incorporation into the nascent protein. Further support for the location of the N-terminal epitope markers may be found at page 42, lines 23-24 and page 48, lines 13-17. Further support for the location of the C-terminal epitope marker may be found at page 48, lines 26-30.

## **II. Claims 1, 9 and 11-13 are not unpatentable under 35 U.S.C. §103(a).**

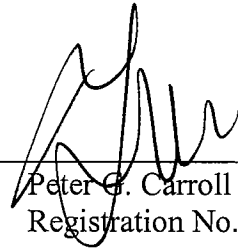
Based on the above arguments regarding the references Little *et al.*, Garvin *et al.* and Knop *et al.*, the Applicants likewise contend that the rejection of Claims 1, 9 and 11-13 based on a further combination with Elion should be withdrawn. Elion is only cited by the Examiner as allegedly teaching primers of certain lengths. Elion does not remedy the above-indicated deficiencies of the combination of Knop with Little/Garvin.

**CONCLUSION**

In view of the above arguments and amendments, the Applicants contend that Claims 1, 9 and 11-13 as well as new Claims 38-41 are in condition for allowance. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned at 781.828.9870

Respectfully submitted,

Dated: September 14, 2009



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